A Review of Uncertainties in the Current IRIS Cancer Unit Risk for Asbestos: Strategies for Uncertainty Analysis in Risk Assessment

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Introduction

The current cancer inhalation unit risk for asbestos was posted on the EPA's Integrated Risk Information System (IRIS) database in 1988 based on the Airborne Asbestos Health Assessment Update (US EPA, 1986). The IRIS Program is undertaking a reassessment providing an update on the current understanding of asbestos carcinogenicity and adjust the inhalation unit risk as needed. Areas where science is more fully understood, or has been refined since the original assessment, may be sources of uncertainty in the current unit risk. Areas of uncertainty in the current unit risk include: potency of different mineral forms, fiber length distribution, exposure duration, smoking status, exposure metric, and possible underestimation of mesothelioma risk.

Derivation of the Current IRIS Inhalation Unit Risk for Asbestos

- Based on epidemiologic data from cohorts exposed to amosite, chrysotile, crocidolite or mixed fiber types
- Combined risk of lung cancer and mesothelioloma
- Combined for smokers and non-smokers,
- Combined for men and women
- Unit risk expressed in f/mL based on fiber counts made by Phased Contrast Microscopy or total dust data converted to PCM fibers.
  - >0.4 µm in diameter
  - >5 µm in length
  - = 3:1 aspect ratio

Lung Cancer: Relative Risk Model

$I_O = I_E \ [1 + K_L * EC(t-10) \ ]$

I_O = Observed incidence in exposed cohort
I_E = Expected incidence without exposure
K_L = Proportionality constant
$E_C(t-10)$ = Cum. Exposure, lagged 10 years

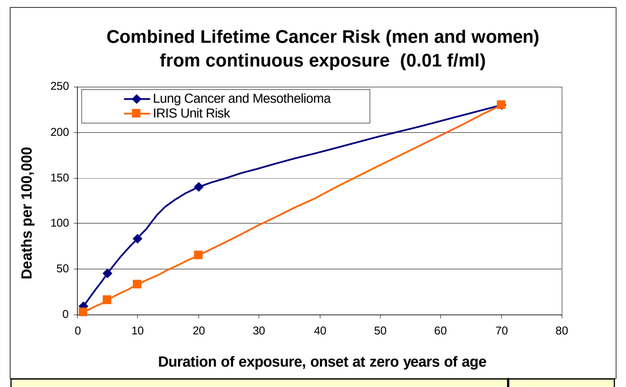
$K_L = 0.010$
Geometric Mean of 11 studies,
(milling and mining studies excluded)

Mesothelioma: Absolute Risk Model

$I_M = 0$ For T< 10 years:
$I_M = K_M * f(T-10)^3$ For 10+d > T > 10 years:
$I_M = K_M * f [(T-10)^3 – (T-10-d)^3]$ For T > 10+d:

I_M = Observed incidence of mesothelioma in exposed cohort
T = Time since onset of exposure
d = Duration of exposure
f = concentration of fibers
K_M = Proportionality constant

$K_M = 1.02 X10^{-8}$
Based on Geometric mean of adjusted K_M of 13 studies
(one study excluded, friction products)



Gender	Deaths/100,000 Mesothelioma	Lung Cancer	Total	Unit Risk	Combined Unit Risk
Female	183	35	218	0.218	
Male	129	114	242	0.242	
All	156	74	230	0.230	**0.23**

Uncertainties Identified by Nicholson,1986

- Exposure estimates were poor
  - ?Limited historical data
  - ?Use of total dust measurements
  - ?Conversion to f/ml
- Fiber length profile varies
- Long chrysotile in mining may not be respirable
- Material not quantified – length and width cutoffs
- Potential for increased potency of amphiboles to induce mesothelioma is not considered separately
- Potential for differential potency for lung cancer
- Effects of smoking status are not considered
- Lifetime risk estimate for less-than-lifetime exposure

Additional Issues Since Unit Risk Development

- Mesothelioma may have been underestimated in earlier cohorts due to length of follow-up
- Amphibloe asbestos believed to be more potent for mesothelioma than chrysotile
- Change in smoking habits impact life table analysis
- Synergistic effect of smoking and asbestos on lung cancer
- Potency of cleavage fragments

Site Specific Areas of Uncertainty

- Mineral present at site (chrysotile, amosite, actinolite, tremolite, Libby amphibole)
- Size distribution of materials at the site (length, width, aspect ratio)
- Presence of cleavage fragments
- Smoking status of population
- Less than lifetime exposure
  - Duration of exposure
  - Early lifetime

Suggested strategy for site specific uncertainty analysis

- Estimate risk using IRIS Unit risk
- Evaluate areas of uncertainty for the site
- Qualitative discussion of uncertainty
- Quantitative analysis
  - Present a range of estimates
  - Age of exposure
  - Alternative quantitative models

Quantitative Tools Available

- Nicholson lifetime risk tables
  - ?Sum risks from source tables based on site specific exposures
  - ?Could be used to address early-lifetime exposures
- Life-table analysis
  - ?Incorporate mineral specific K_L and/or K_M
  - ?Could be used to address early-lifetime exposures
  - ?May address updated smoking statistics or mortality data
- Alternative Models
  - ?Hodgson and Darnton (Lung cancer and mesothelioma)
  - ?Stayner (Chrysotile only)
  - ?OSWER Risk Methodology (under development)

Scenario 1

Material: Predominately chrysotile asbestos from insulation or other building materials
Exposure: Chronic (30 years), continuous or repeated intermittent (e.g. work day)
Target population: infants, children and adults
Evaluation:
Similar materials to source data for unit risk
- ?Distribution of fiber dimensional characteristic
- ?Mineral form

Exposure regimen similar
Early-lifetime exposure included

Recommended Approach:
1) Standard risk calculation, IRIS unit risk
2) Qualitative Uncertainty Analysis
Early lifetime exposure: Qualitative discussion, since exposure involves primarily chrysotile

Scenario 2

Material: Amphibole asbestos from demolition of asbestos containing building materials
Exposure: Chronic (30 years), continuous residential exposure
Target population: infants, children and adults
Evaluation:
Similar materials to source data for unit risk
- ?Distribution of fiber dimensional characteristic
- ?Mineral form - Amphibole asbestos predominates

Exposure regimen is continuous,
versus repeated intermittent
Early-lifetime exposure included

Recommended Approach:
1) Standard risk calculation using IRIS unit risk
2) Quantitative Uncertainty Analysis
Additional calculation of lifetime cancer risk
- ?Include early-lifetime exposure
- ?Estimate risk from lifetime risk tables (EPA1986)

Scenario 3

Material: Naturally occurring Amphibole asbestos
Exposure: Recreational intermittent peak, over 20 years
Target population: Children and adults
Evaluation:
Materials dissimilar to source data for unit risk
- ?Aspect ratio
- ?Fiber length/ width distributions
- ?Mineralogy – not commercially used

Exposure regimen very different from occ. cohorts
Early-lifetime exposure included

Recommended Approach:
1) Standard risk calculation using IRIS unit risk
2) Quantitative Uncertainty Analysis
Life-table analysis for risk estimates
- ?Include early-lifetime exposure
- ?Adjust for amphibole exposure

3) Qualitative Discussion of Additional Uncertainties
- ?Fiber dimensional characteristics
- ?Mineral form of material is slightly different
- ?Peak intermittent exposures

* The views expressed in this abstract are those of the authors and do not necessarily reflect the views or policies of the US Environmental Protection Agency.